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EFFECTS OF SUBCHRONIC PATERNAL EXPOSURE TO CYCLOPHOSPHAMIDE AND ACROLEIN ON MALE FERTILITY AND EARLY EMBRYONIC DEVELOPMENT IN RATS

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The purpose of the present studies was to investigate the effects of subchronic paternal treatment of cyclophosphamide (CP) and acrolein on male fertility and early embryonic development. Two approaches were pursued. The first was to perform in vivo test for observing the adverse effects of CP and acrolein on the function og male reproductive system and pregnancy outcome. Saline (control), 1 of 3 doses of CP (0.2, 1, and 5 mg/kg bw) or 1 of 2 doses of acrolein (0.2 and 1 mg/kg bw) was given daily by gavage to groups of 15 adult male SD rats for 4 weeks. At the end of pre-treatment period, males were mated overnight with untreatment females. Following morning, the presence of sperm was examined in vaginal smear and males demonstrating successful induction of pregnancy were sacrificed on that day to assess sperm parameters and histopathology of reproductive organs. The resulting pregnant females were sacrificed on day 20 of gestation to evaluate pregnancy outcome. As a result, four-week paternal administration with CP resulted in adverse effects on male fertility and pregnancy outcome without remarkable histopathological changes in testes and epididymides; sperm numbers, sperm motility, copulation index and fertility index were markedly decreased in the group treated with 5 mg/kg bw and numbers of live fetuses showed steep dose-response curves. Interestingly, the male mediated adverse consquences of acrolein was not similar to those of CP. The second was to investigate if apoptosis in testes plays an important role in madiating adverse effect of CO and acrolein. Apoptosis was assessed in testes by TUNEL assay and confirmed by DNA fragmentation assay. No effect was observed on apoptosis induction in testes treated with low doses of CP or acrolein for 4 weeks. In contrast, a single exposure to high doses of CP or acrolein increased apoptosis in testes. Taken together, the results indicated the followings: (1)